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Sequence Listing was accepted.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866)
217-9197 (toll free).

Reviewer: markspencer

Timestamp: [year=2008; month=10; day=10; hr=9; min=32; sec=25; ms=908;]

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Application No: 10658834 Version No: 5.0

Input Set:

Output Set:

Started: 2008-08-27 18:29:50.675
Finished: 2008-08-27 18:30:41.822
Elapsed: 0 hr(s) 0 min(s) 51 sec(s) 147 ms
Total Warnings: 198
Total Errors: 88
No. of SeqIDs Defined: 1306
Actual SeqID Count: 1306

Error code	Error Description
W 213	Artificial or Unknown found in <213> in SEQ ID (2)
W 213	Artificial or Unknown found in <213> in SEQ ID (3)
W 213	Artificial or Unknown found in <213> in SEQ ID (4)
W 213	Artificial or Unknown found in <213> in SEQ ID (5)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (5)
W 213	Artificial or Unknown found in <213> in SEQ ID (6)
W 213	Artificial or Unknown found in <213> in SEQ ID (7)
W 213	Artificial or Unknown found in <213> in SEQ ID (8)
W 213	Artificial or Unknown found in <213> in SEQ ID (9)
W 213	Artificial or Unknown found in <213> in SEQ ID (10)
W 213	Artificial or Unknown found in <213> in SEQ ID (11)
W 213	Artificial or Unknown found in <213> in SEQ ID (12)
W 213	Artificial or Unknown found in <213> in SEQ ID (13)
W 213	Artificial or Unknown found in <213> in SEQ ID (14)
W 213	Artificial or Unknown found in <213> in SEQ ID (15)
W 213	Artificial or Unknown found in <213> in SEQ ID (16)
W 213	Artificial or Unknown found in <213> in SEQ ID (17)
W 213	Artificial or Unknown found in <213> in SEQ ID (18)
E 355	Empty lines found between the amino acid numbering and the

Input Set:

Output Set:

Started: 2008-08-27 18:29:50.675
Finished: 2008-08-27 18:30:41.822
Elapsed: 0 hr(s) 0 min(s) 51 sec(s) 147 ms
Total Warnings: 198
Total Errors: 88
No. of SeqIDs Defined: 1306
Actual SeqID Count: 1306

Error code	Error Description
E 321	No. of Bases conflict, this line has no nucleotides SEQID (18)
W 213	Artificial or Unknown found in <213> in SEQ ID (19)
W 213	Artificial or Unknown found in <213> in SEQ ID (20)
W 213	Artificial or Unknown found in <213> in SEQ ID (21) This error has occurred more than 20 times, will not be displayed
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (44)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (63)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (84)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (97)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (105)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (149)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (188)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (237)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (238)

Input Set:

Output Set:

Started: 2008-08-27 18:29:50.675
Finished: 2008-08-27 18:30:41.822
Elapsed: 0 hr(s) 0 min(s) 51 sec(s) 147 ms
Total Warnings: 198
Total Errors: 88
No. of SeqIDs Defined: 1306
Actual SeqID Count: 1306

Error code	Error Description
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (274)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (332)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (377)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (386)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (441)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (478)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (522)
E 355	Empty lines found between the amino acid numbering and the
E 321	No. of Bases conflict, this line has no nucleotides SEQID (533)
E 355	Empty lines found between the amino acid numbering and the proteins
E 321	No. of Bases conflict, this line has no nucleotides SEQID (564) POS (112)

SEQUENCE LISTING

<110> Gantier, Rene
Guyon, Thierry
Drittanti, Lila
Vega, Manuel

<120> RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY, THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES

<130> 119365-00005/922

<140> 10658834

<141> 2003-09-08

<150> 60/457,135

<151> 2003-03-21

<150> 60/409,898

<151> 2002-09-09

<160> 1306

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<210> 1

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<212> PRT

<213> Homo sapiens

<400> 1

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Leu	Leu	Ala	Gln	Met	Arg	Arg	Ile	Ser	Leu	Phe	Ser	Cys	Leu	Lys	Asp
			20					25					30		
Arg	His	Asp	Phe	Gly	Phe	Pro	Gln	Glu	Glu	Phe	Gly	Asn	Gln	Phe	Gln
		35					40					45			
Lys	Ala	Glu	Thr	Ile	Pro	Val	Leu	His	Glu	Met	Ile	Gln	Gln	Ile	Phe
	50					55					60				
Asn	Leu	Phe	Ser	Thr	Lys	Asp	Ser	Ser	Ala	Ala	Trp	Asp	Glu	Thr	Leu
65					70					75					80
Leu	Asp	Lys	Phe	Tyr	Thr	Glu	Leu	Tyr	Gln	Gln	Leu	Asn	Asp	Leu	Glu
				85					90					95	
Ala	Cys	Val	Ile	Gln	Gly	Val	Gly	Val	Thr	Glu	Thr	Pro	Leu	Met	Lys
			100					105					110		
Glu	Asp	Ser	Ile	Leu	Ala	Val	Arg	Lys	Tyr	Phe	Gln	Arg	Ile	Thr	Leu
	115						120					125			
Tyr	Leu	Lys	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val	Arg
	130					135					140				
Ala	Glu	Ile	Met	Arg	Ser	Phe	Ser	Leu	Ser	Thr	Asn	Leu	Gln	Glu	Ser
145					150					155					160
Leu	Arg	Ser	Lys	Glu											
				165											

<210> 2

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> D2A Mutant IFN-alpha 2b

<400> 2

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Cys Ala Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1          5          10          15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
          20          25          30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
          35          40          45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
          50          55          60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65          70          75          80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
          85          90          95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
          100          105          110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
          115          120          125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
          130          135          140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145          150          155          160
Leu Arg Ser Lys Glu
          165
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<210> 3

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> P4A Mutant IFN-alpha 2b

<400> 3

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 1          5          10          15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
          20          25          30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
          35          40          45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
          50          55          60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65          70          75          80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
          85          90          95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
          100          105          110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
          115          120          125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
          130          135          140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
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145 150 155 160
 Leu Arg Ser Lys Glu
 165
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 <213> Artificial Sequence

 <220>
 <223> Q5A Mutant IFN-alpha 2b

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 1 5 10 15
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 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
 100 105 110
 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
 115 120 125
 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
 130 135 140
 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
 145 150 155 160
 Leu Arg Ser Lys Glu
 165

<210> 5
 <211> 165
 <212> PRT
 <213> Artificial Sequence

<220>

<223> T6A Mutant IFN-alpha 2b

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 1 5 10 15
 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 20 25 30
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35 40 45
 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50 55 60
 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
 65 70 75 80
 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
 85 90 95
 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys

100	105	110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu		

115	120	125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg		
130	135	140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser		
145	150	155
Leu Arg Ser Lys Glu		160

165

<210> 6

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> H7A Mutant IFN-alpha 2b

<400> 6

Cys Asp Leu Pro Gln Thr Ala Ser Leu Gly Ser Arg Arg Thr Leu Met		
1	5	10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp		15
20	25	30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln		
35	40	45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe		
50	55	60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu		
65	70	75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu		80
85	90	95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys		
100	105	110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu		
115	120	125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg		
130	135	140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser		
145	150	155
Leu Arg Ser Lys Glu		160

165

<210> 7

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> S8A Mutant IFN-alpha 2b

<400> 7

Cys Asp Leu Pro Gln Thr His Ala Leu Gly Ser Arg Arg Thr Leu Met		
1	5	10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp		15
20	25	30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln		
35	40	45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe		

50		55		60											
Asn	Leu	Phe	Ser	Thr	Lys	Asp	Ser	Ser	Ala	Ala	Trp	Asp	Glu	Thr	Leu
65					70				75						80
Leu	Asp	Lys	Phe	Tyr	Thr	Glu	Leu	Tyr	Gln	Gln	Leu	Asn	Asp	Leu	Glu
			85						90					95	
Ala	Cys	Val	Ile	Gln	Gly	Val	Gly	Val	Thr	Glu	Thr	Pro	Leu	Met	Lys
		100						105					110		
Glu	Asp	Ser	Ile	Leu	Ala	Val	Arg	Lys	Tyr	Phe	Gln	Arg	Ile	Thr	Leu
		115					120					125			
Tyr	Leu	Lys	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val	Arg
	130					135					140				
Ala	Glu	Ile	Met	Arg	Ser	Phe	Ser	Leu	Ser	Thr	Asn	Leu	Gln	Glu	Ser
145					150					155					160
Leu	Arg	Ser	Lys	Glu											
				165											

<210> 8

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> L9A Mutant IFN-alpha 2b

<400> 8

Cys	Asp	Leu	Pro	Gln	Thr	His	Ser	Ala	Gly	Ser	Arg	Arg	Thr	Leu	Met
1				5					10					15	
Leu	Leu	Ala	Gln	Met	Arg	Arg	Ile	Ser	Leu	Phe	Ser	Cys	Leu	Lys	Asp
		20						25					30		
Arg	His	Asp	Phe	Gly	Phe	Pro	Gln	Glu	Glu	Phe	Gly	Asn	Gln	Phe	Gln
		35					40					45			
Lys	Ala	Glu	Thr	Ile	Pro	Val	Leu	His	Glu	Met	Ile	Gln	Gln	Ile	Phe
	50					55					60				
Asn	Leu	Phe	Ser	Thr	Lys	Asp	Ser	Ser	Ala	Ala	Trp	Asp	Glu	Thr	Leu
65					70				75						80
Leu	Asp	Lys	Phe	Tyr	Thr	Glu	Leu	Tyr	Gln	Gln	Leu	Asn	Asp	Leu	Glu
			85						90					95	
Ala	Cys	Val	Ile	Gln	Gly	Val	Gly	Val	Thr	Glu	Thr	Pro	Leu	Met	Lys
		100						105					110		
Glu	Asp	Ser	Ile	Leu	Ala	Val	Arg	Lys	Tyr	Phe	Gln	Arg	Ile	Thr	Leu
		115					120					125			
Tyr	Leu	Lys	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val	Arg
	130					135					140				
Ala	Glu	Ile	Met	Arg	Ser	Phe	Ser	Leu	Ser	Thr	Asn	Leu	Gln	Glu	Ser
145					150					155					160
Leu	Arg	Ser	Lys	Glu											
				165											

<210> 9

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> G10A Mutant IFN-alpha 2b

<400> 9

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 1              5              10              15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
      20              25              30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35              40              45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50              55              60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65              70              75              80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
      85              90              95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
      100              105              110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
      115              120              125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
      130              135              140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
      145              150              155              160
Leu Arg Ser Lys Glu
      165
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<210> 10

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> S11A Mutant IFN-alpha 2b

<400> 10

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 1              5              10              15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
      20              25              30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
 35              40              45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
 50              55              60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65              70              75              80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
      85              90              95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
      100              105              110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
      115              120              125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
      130              135              140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
      145              150              155              160
Leu Arg Ser Lys Glu
      165
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<210> 11

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> R12A Mutant IFN-alpha 2b

<400> 11

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Ala Arg Thr Leu Met
 1           5           10           15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
          20           25           30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
          35           40           45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
          50           55           60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65           70           75           80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
          85           90           95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
          100          105          110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
          115          120          125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
          130          135          140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145          150          155          160
Leu Arg Ser Lys Glu
          165
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<210> 12

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> R13A Mutant IFN-alpha 2b

<400> 12

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 1           5           10           15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
          20           25           30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
          35           40           45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
          50           55           60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65           70           75           80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
          85           90           95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
          100          105          110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
          115          120          125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
```

130

135

140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn